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Percutaneous Vertebroplasty for Treatment of Painful Osteoporotic Vertebral Compression Fractures

An Evidence-Based Analysis

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List of Abbreviations

BK	Balloon kyphoplasty
CI	Confidence interval(s)
CT	Conservative treatment
ITT	Intention to treat
MCID	Minimal clinically important difference
MAS	Medical Advisory Secretariat
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
PCE	Pulmonary cement embolism
PO	Primary outcome
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
VCF	Vertebral compression fracture
VP	Vertebroplasty

Executive Summary

Objective of Analysis

The objective of this analysis is to examine the safety and effectiveness of percutaneous vertebroplasty for treatment of osteoporotic vertebral compression fractures (VCFs) compared with conservative treatment.

Clinical Need and Target Population

Osteoporosis and associated fractures are important health issues in ageing populations. Vertebral compression fracture secondary to osteoporosis is a cause of morbidity in older adults. VCFs can affect both genders, but are more common among elderly females and can occur as a result of a fall or a minor trauma. The fracture may occur spontaneously during a simple activity such as picking up an object or rising up from a chair. Pain originating from the fracture site frequently increases with weight bearing. It is most severe during the first few weeks and decreases with rest and inactivity.

Traditional treatment of painful VCFs includes bed rest, analgesic use, back bracing and muscle relaxants. The comorbidities associated with VCFs include deep venous thrombosis, acceleration of osteopenea, loss of height, respiratory problems and emotional problems due to chronic pain.

Percutaneous vertebroplasty is a minimally invasive surgical procedure that has gained popularity as a new treatment option in the care for these patients. The technique of vertebroplasty was initially developed in France to treat osteolytic metastasis, myeloma, and hemangioma. The indications were further expanded to painful osteoporotic VCFs and subsequently to treatment of asymptomatic VCFs.

The mechanism of pain relief, which occurs within minutes to hours after vertebroplasty, is still not known. Pain pathways in the surrounding tissue appear to be altered in response to mechanical, chemical, vascular, and thermal stimuli after the injection of the cement. It has been suggested that mechanisms other than mechanical stabilization of the fracture, such as thermal injury to the nerve endings, results in immediate pain relief.

Percutaneous Vertebroplasty

Percutaneous vertebroplasty is performed with the patient in prone position and under local or general anesthesia. The procedure involves fluoroscopic imaging to guide the injection of bone cement into the fractured vertebral body to support the fractured bone. After injection of the cement, the patient is placed in supine position for about 1 hour while the cement hardens.

Cement leakage is the most frequent complication of vertebroplasty. The leakages may remain asymptomatic or cause symptoms of nerve irritation through compression of nerve roots. There are several reports of pulmonary cement embolism (PCE) following vertebroplasty. In some cases, the PCE may remain asymptomatic. Symptomatic PCE can be recognized by their clinical signs and symptoms such as chest pain, dyspnea, tachypnea, cyanosis, coughing, hemoptysis, dizziness, and sweating.

Research Methods

Literature Search

A literature search was performed on Feb 9, 2010 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cumulative Index to Nursing & Allied Health Literature

(CINAHL), the Cochrane Library, and the International Agency for Health Technology Assessment (INAHTA) for studies published from January 1, 2005 to February 9, 2010.

Studies were initially reviewed by titles and abstracts. For those studies meeting the eligibility criteria, full-text articles were obtained and reviewed. Reference lists were also examined for any additional relevant studies not identified through the search. Articles with an unknown eligibility were reviewed with a second clinical epidemiologist and then a group of epidemiologists until consensus was established. Data extraction was carried out by the author.

Inclusion Criteria

- Study design: Randomized controlled trials (RCTs) comparing vertebroplasty with a control group or other interventions
- Study population: Adult patients with osteoporotic vertebral fractures
- Study sample size: Studies included 20 or more patients
- English language full-reports
- Published between Jan 1 2005 and Feb 9 , 2010
- (eligible studies identified through the Auto Alert function of the search were also included)

Exclusion Criteria

- Non-randomized studies
- Studies on conditions other than VCF (e.g. patients with multiple myeloma or metastatic tumors)
- Studies focused on surgical techniques
- Studies lacking outcome measures

Results of Evidence-Based Analysis

A systematic search yielded 168 citations. The titles and the abstracts of the citations were reviewed and full text of the identified citations was retrieved for further consideration. Upon review of the full publications and applying the inclusion and exclusion criteria, 5 RCTs were identified. Of these, two compared vertebroplasty with sham procedure, two compared vertebroplasty with conservative treatment, and one compared vertebroplasty with balloon kyphoplasty.

Randomized Controlled Trials

Recently, the results of two blinded randomized placebo-controlled trials of percutaneous vertebroplasty were reported. These trials, providing the highest quality of evidence available to date, do not support the use of vertebroplasty in patients with painful osteoporotic vertebral compression fractures. Based on the results of these trials, vertebroplasty offer no additional benefit over usual care and is not risk free.

In these trials the treatment allocation was blinded to the patients and outcome assessors. The control group received a sham procedure simulating vertebroplasty to minimize the effect of expectations and to reduce the potential for bias in self-reporting of outcomes. Both trials applied stringent exclusion criteria so that the results are generalizable to the patient populations that are candidates for vertebroplasty. In both trials vertebroplasty procedures were performed by highly skilled interventionists. Multiple valid outcome measures including pain, physical, mental, and social function were employed to test the between group differences in outcomes.

Prior to these two trials, there were two open randomized trials in which vertebroplasty was compared with conservative medical treatment. In the first randomized trial, patients were allowed to cross over to the other arm and had to be stopped after two weeks due to the high numbers of patients crossing over. The other study did not allow cross over and recently published the results of 12 months follow-up.

The following is the summary of the results of these 4 trials:

Two blinded RCTs on vertebroplasty provide the highest level of evidence available to date. Results of these two trials are supported by findings of an open randomized trial with 12 months follow-up. Blinded RCTs showed:

- No significant differences in pain scores of patients who received vertebroplasty and patients who received a sham procedure as measured at 3 days, 2 weeks and 1 month in one study and at 1 week, 1 month, 3 months, and 6 months in the other.
- The observed differences in pain scores between the two groups were neither statistically significant nor clinically important at any time points.
- The above findings were consistent with the findings of an open RCT in which patients were followed for 12 months. This study showed that improvement in pain was similar between the two groups at 3 months and were sustained to 12 months.
- In the blinded RCTs, physical, mental, and social functioning were measured at the above time points using 4-5 of the following 7 instruments: RDQ, EQ-5D, SF-36 PCS, SF-36 MCS, AQoL, QUALEFFO, SOF-ADL
- There were no significant differences in any of these measures between patients who received vertebroplasty and patients who received a sham procedure at any of the above time points (with a few exceptions in favour of control intervention).
- These findings were also consistent with the findings of an open RCT which demonstrated no significant between group differences in scores of ED-5Q, SF-36 PCS, SF 36 MCS, DPQ, Barthel, and MMSE which measure physical, mental, and social functioning (with a few exceptions in favour of control intervention).
- One small (n=34) open RCT with a two week follow-up detected a significantly higher improvement in pain scores at 1 day after the intervention in vertebroplasty group compared with conservative treatment group. However, at 2 weeks follow-up, this difference was smaller and was not statistically significant.
- Conservative treatment was associated with fewer clinically important complications
- Risk of new VCFs following vertebroplasty was higher than those in conservative treatment but it requires further investigation.

Background

Objective of Analysis

The objective of this analysis is to examine the safety and effectiveness of percutaneous vertebroplasty for treatment of osteoporotic vertebral compression fractures compared with conservative treatment.

Clinical Need and Target Population

Osteoporosis and associated fractures are important health issues in ageing populations. Vertebral compression fracture secondary to osteoporosis is a cause of morbidity in older adults. VCFs can affect both genders but are more common among elderly females and can occur as a result of a fall or a minor trauma. The fracture may occur spontaneously during a simple activity such as picking up an object or rising up from a chair. Pain originating from the fracture site frequently increases with weight bearing. It is most severe during the first few weeks, and decreases with rest and inactivity. (1)

Traditional treatment of painful VCFs includes bed rest, analgesic use, back bracing, and muscle relaxants. The comorbidities associated with VCFs include deep venous thrombosis, acceleration of osteopenea, loss of height, respiratory problems and emotional problems due to chronic pain.

Percutaneous vertebroplasty is a minimally invasive surgical procedure that has gained popularity as a new treatment option in the care for these patients. The technique of vertebroplasty was initially developed in France to treat osteolytic metastasis, myeloma, and hemangioma. The indications were further expanded to painful osteoporotic VCFs and subsequently to treatment of asymptomatic VCFs.

The mechanism of pain relief, which occurs within minutes to hours after vertebroplasty, is still not known. (2) Pain pathways in the surrounding tissue appear to be altered in response to mechanical, chemical, vascular, and thermal stimuli after the injection of the cement. It has been suggested that mechanisms other than mechanical stabilization of the fracture, such as thermal injury to the nerve endings, results in immediate pain relief. (3)

Percutaneous Vertebroplasty

Percutaneous vertebroplasty is performed with the patient in prone position and under local or general anesthesia. The procedure involves fluoroscopic imaging to guide the injection of bone cement into the fractured vertebral body to support the fractured bone. After injection of the cement, the patient is placed in supine position for about 1 hour while the cement hardens.

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Evidence-Based Analysis

Research Questions

For the treatment of painful osteoporotic VCFs:

- Does vertebroplasty provide a better pain relief than a conservative approach or other interventions?
- Does vertebroplasty provide more improvement in physical, mental, and social functioning than a conservative approach or other interventions?
- How safe is vertebroplasty?

Research Methods

Literature Search

Search Strategy

A literature search was performed on Feb 9, 2010 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Cochrane Library, and the International Agency for Health Technology Assessment (INAHTA) for studies published from January 1, 2005 to February 9, 2010. The search was updated on Aug 9, 2010 to ensure that no literature meeting the inclusion criteria had been published since the initial search date.

Studies were initially reviewed by titles and abstracts. For those studies meeting the eligibility criteria, full-text articles were obtained and reviewed. Reference lists were also examined for any additional relevant studies not identified through the search. Articles with an unknown eligibility were reviewed with a second clinical epidemiologist and then a group of epidemiologists until consensus was established. Data extraction was carried out by the author.

Inclusion Criteria

- Study design: RCTs comparing vertebroplasty with a control group or other interventions
- Study population: Adult patients with osteoporotic vertebral fractures
- Study sample size: Studies included 20 or more patients
- English language full-reports
- Published between Jan 1 2005 and Feb 9 , 2010
- (eligible studies identified through the Auto Alert function of the search were also included)

Exclusion Criteria

- Non-randomized studies
- Studies on conditions other than VCF (e.g. patients with multiple myeloma or metastatic tumors)
- Studies focused on surgical techniques
- Studies lacking outcome measures

Outcomes of Interest

Primary Outcome

- Changes in back-related pain scores

Secondary Outcomes

- Changes in scores related to disability (Physical functioning scores)
- Changes in scores related to mental and social functioning
- Incidence of new VCFs
- Incidence of cement leakage and subsequent neurological adverse events

Statistical Analysis

For comparison of scores, mean differences and 95% confidence intervals (CI) at the baseline and at different time points after the intervention were recorded and compared. The minimal clinically important difference (MCID) for various scores was identified through the literature and used as a tool to measure the degree to which the differences in scores are clinically important.

Quality of Evidence

Quality of the Randomized Controlled Trials

Jadad instrument (4) was used to determine the quality of the RCTs on vertebroplasty in terms of how they were designed and how they were conducted. This instrument is recommended by Cochrane Musculoskeletal Group in the preparation of their Cochrane systematic reviews and is the only instrument that has been constructed according to psychometric principles. Jadad scale uses a simple and easy to understand approach that incorporates the most important components of methodological quality; randomization, blinding, and handling of patient attrition. This instrument has been used extensively in musculoskeletal research. (5)

Quality of Body of Evidence

The quality of the body of evidence was assessed as high, moderate, low, or very low according to the GRADE Working Group criteria. (6) Four key elements of the GRADE system are study design, study quality, consistency, and directness. The description of the 4 elements is:

1. Study design refers to the basic design of the study and has broadly categorized as observational studies and randomized trials.

2. Quality refers to the detailed study method and execution. For RCTs, for example, adequacy of allocation, concealment, and blinding must be taken into account in determining the study quality.

3. Consistency refers to the similarity of estimates of effect across studies. If there are important and unexplained inconsistencies in the results, our confidence in the estimate of effect for that outcome decreases. Differences in the direction of effect, the size of the differences in effect, and the significance of the differences guide the decision about whether important inconsistency exists.

4. Directness refers to the extent to which the interventions and outcome measures are similar to those of interest. For example, there may be uncertainty about the directness of the evidence if people of interest are older or sicker that the study population.

As stated by the GRADE Working Group, the following definitions of quality were used in grading the quality of the evidence:

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain

Results of Evidence-Based Analysis

A systematic search yielded 168 citations (Search strategy is available in Appendix 1). The titles and the abstracts of the citations were reviewed and full text of the identified citations was retrieved for further consideration. Upon review of the full publications and applying the inclusion and exclusion criteria, 5 RCTs were identified. (7-11) Of these, two (7;8) compared vertebroplasty with sham procedure, two compared vertebroplasty with conservative treatment (9;10), and one (11) compared vertebroplasty with balloon kyphoplasty. (Table 1).

Table 1: Quality of Evidence of Included Studies: Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Study Design	Level of Evidence†	Number of Eligible Studies
Large RCT, systematic review of RCTs	1	3
Large RCT unpublished but reported to an international scientific meeting	1(g)	0
Small RCT	2	2
Small RCT unpublished but reported to an international scientific meeting	2(g)	N/A
Non-RCT with contemporaneous controls	3a	N/A
Non-RCT with historical controls	3b	N/A
Non-RCT presented at international conference	3(g)	N/A
Surveillance (database or register)	4a	N/A
Case series (multisite)	4b	N/A
Case series (single site)	4c	N/A
Retrospective review, modelling	4d	N/A
Case series presented at international conference	4(g)	N/A
	Total	**5**

(12); RCT refers to randomized controlled trial

The authors of one study (9) published their 12 month follow-up. (13) This information was also considered in this assessment.

All studies included patients with painful VCFs and the mean age of patients ranged from 72 to 80 years. The duration of follow- up varied across the studies, ranging from 2 weeks to 12 months. The study population ranged from 34 to 131 patients. Study characteristics are shown in Table 2.

Table 2. Study Characteristics: Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Study (Study period)	Centres	Comparison Arms	Design	Power /Analysis	Cross Over Permitted N (%)	Patients, N	(Mean Age, SD/Range)	Duration of back pain/Fracture age	Follow-up, N
Liu et al. 2010(11)	Taiwan	PV vs BK	RCT	Power: NR Analysis: as treated	No	100 PV: 50 CI: 50	BK: 72.3±7.6 PV: 74.3±6.4	Within 43 days of injury	6 months
Kallmes et al. 2009(7) INVEST Trial (June 2004-Aug 2008)	5 in US 5 in UK 1 in AU	PV vs sham	RCT Multicentre Double-blind	Power: >80% for primary outcomes Analysis: ITT	1 month after intervention < 1 month: PV: 1 (1) CI: 2 (3) >=3 months PV: 8 (12) CI: 27 (43) P<0.001	131 PV: 68 CI: 63	PV: 73.4±9.4 CI: 74.3±9.6	<1 year 41% were <= 13 weeks	3 months: PV: 64 CI: 61
Buchbinder et al. 2009(8) Australian New Zealand Trial	4 in AU	PV vs sham	RCT Multicentre Double-blind	Power: 80% for primary outcomes Analysis: ITT	No	78 PV:38 CI: 40	PV: 74.2±14 CI: 78.9±9.5	<=1 year 32% were < 6 weeks	6 months: PV: 35 CI: 36
Rousing et al. 2009(9) & 2010(13)	Denmark	PV vs conservative treatment	RCT	Power: 80% Analysis: as treated	No	50* PV: 25 CI: 24	PV: 80 (65-96) CI: 80 (71-93)	Acute (< 2 weeks, n=40) Subacute (2-8 weeks, n=10)	3 months: PV: 24 CI: 23 12 months: PV: 23 CI: 22
Voormolen et al. 2007(10) VERTOS trial	The Netherlands	PV vs optimal pain management	RCT 3 centres	Analysis: ITT	2 weeks after treatment CI: 14 (88%)	34 PV: 18 CI: 16	PV: 72 (59-84) CI: 74 (55-88)	At least 6 weeks but no longer than 6 months	No follow-up

* One patient refused to participate in the study after surgery and was excluded; RCT, Randomized controlled trial; PV, Percutaneous vertebroplasty; CI, Control intervention; ITT, Intention to treat

Open Randomized Trials

The first RCT (10) comparing the effectiveness of vertebroplasty with those of optimal pain medication was published in 2007. The intention of this study was to follow the patients from both groups for 1 year with MR imaging scans and standardized questionnaires. It was planned to gather respective data for the following intervals: 1 day, 2 weeks, 3 months, 6 months, and 12 months. However, the design of the study allowed patients in the optimal pain medication group to cross over to the vertebroplasty arm if they still had severe pain 2 weeks after receiving medical treatment. Unexpectedly, 14 of the 16 patients (88%) in the control arm requested treatment by vertebroplasty two weeks after initiation of medical treatment. Since the high rate of cross over interfered with the interest of the study to compare the two treatment, the study had to be stopped because the outcomes would not be comparable. Therefore, the follow-up data from 2 weeks after the start of treatment were not analyzed. This study showed a significant reduction in pain scores 1 day after vertebroplasty compared to the scores in control group. The outcomes concerning two week treatment showed no statistically significant difference in pain scores between the two groups but the quality of life scores (QUALEFFO) and RDQ scores were significantly better in vertebroplasty group compared with control group.

This high rate of cross over in Voormolen's study (10) can be explained by the fact that the mean duration of back pain from vertebral compression fracture in the study population was nearly 3 months and potential candidates for this study were already treated with various conservative therapies. Previously published case series studies on vertebroplasty reported a significant pain reduction following the procedure; this knowledge may have influenced the patients' decision to cross over to the other arm to receive a presumably more effective treatment.

As a result, the authors of the first RCT on vertebroplasty suggested that for future RCTs, inclusion of patients in an earlier stage after initial fracture is necessary because participants will more readily accept randomization to conservative treatment. The authors also suggested that enrolment of larger groups of patients is necessary to have less influence on the clinical outcome by patients in whom an early healing within 6-8 weeks may take place. Two other important suggestions were "no cross over" from one arm to another; and conducting a sham trial to exclude the influence of other factors such as placebo effect. It was then suggested that both arms should receive percutaneous needle placement; one with cement injection and one without, in order to blind the patients to the actual treatment they receive.

The second RCT on vertebroplasty was conducted by Rousing et al. (9). In this study 50 patients were included and 49 were randomized to either vertebroplasty or conservative treatment. No cross over was allowed but patients were not blinded to the treatment they received. This study reported a 3 months follow-up in 2009 and a 12 months follow-up in 2010. Patients in the control treatment arm had significantly higher pain scores at the baseline compared with those in vertebroplasty arm (P = .02). Vertebroplasty resulted in a significant reduction in pain 1 day after the procedure as compared with the baseline scores. Both groups had significantly lower pain scores compared to the baseline scores at 3 months follow-up (both P = .00).

No significant differences were observed between the groups concerning pain at 3 and 12 months follow-up. There was also no significant differences in other health measures indicated in Table 5 except for the subscale of work/leisure of Dallas Pain Questionnaire (DPQ) at 3 and 12 months (P = .04), and Barthel Index at 12 months (P = .02), both in favour of control group. (Table 5)

The first two open randomized trials provided sufficient evidence to shed light on the design of future RCTs. Following these two preliminary trials, the first two independently conducted and blinded RCTs (7;8) that used sham surgery rather than conventional conservative treatment as the control provided the highest level of evidence available to date.

Double Blinded Randomized Trials

There were two study groups in these trials: patients who received vertebroplasty and patients who received a sham procedure simulating vertebroplasty as control intervention. The results of these two trials showed that although vertebroplasty is highly effective in reducing back pain shortly after the procedure. The natural history of vertebral fractures allows healing to occur within a few weeks resulting in a significant reduction in pain comparable to those achieved by vertebroplasty.

Both studies were published in August 2009, one (7) was conducted in the US [Investigational Vertebroplasty Efficacy and Safety Trial (INVEST trial)], and the other (8) in Australia (Australian New Zealand Clinical Trial).

Kallmes et al. (7) conducted a multicentre double-blinded randomized trial using a sham procedure as control intervention. In this study, a total of 1,813 patients were assessed for eligibility, from which 1, 382 were excluded according to the exclusion criteria.

The inclusion criteria were:

At least 50 years old
1-3 painful VCF at levels of T4 to L5 confirmed with a physical examination and radiographic imaging
Fractures < 12 months
A subjective pain rating of 3 or more on a scale from 0 to 10
Confirmed diagnosis of osteoporosis or osteopnea

The exclusion criteria were:

Malignant tumor deposit (multiple myeloma)
Tumor mass or tumor extension into epidural space at the level of the fracture
Malignancy
Pedicle fracture
Substantial retropulsion of bony fragments
Cord compression
Recent surgery (within 60 days)
Local or systemic infection
Concomitant hip fracture
Uncorrectable bleeding diatheses
Contraindication to conscious sedation
Pregnancy
Dementia
No access to the telephone
Inability to communicate in English well enough to answer all health questions

Applying these exclusion criteria, which were similar to the exclusion criteria of the other vertebroplasty studies, resulted in exclusion of 368 patients who had a tumor, 201patients who had no VCF, 111 patients who had pain level < 3 points, 104 patients who did not have osteoporosis, 102 patients who had coagulopathy, 92 patients who had dementia, and 404 patients who had other exclusion criteria. A total of 300 patients (16.5%) declined to participate. As a result of the stringent exclusion criteria, many patients were excluded and 131 underwent randomization (vertebroplasty 68, sham 63).

The study initially had a power of more than 80% to detect both primary and secondary outcomes in 250 patients, with a two-tailed alpha of .05 considering a 2.5 points difference on the RDQ scores and a 1 point difference on the pain rating. However, the recruitment was slow and a planned interim analysis of

the 90 patients showed that a target sample size of 130 patients would provide more than 80% power to detect a difference in primary outcome measures that is clinically meaningful. Generally, earlier follow-ups are expected to demonstrate a larger difference in scores between the two groups and the later follow-ups to demonstrate a smaller difference due to the natural course of the disease and the healing process that occurs over time. Therefore, the revised sample size calculation based on clinically important differences (MCID of 1.5 points for pain and 3 points for RDQ) appears justified and reasonable to provide sufficient power to test the hypothesis for primary outcomes at one month.

For both interventions the skin and subcutaneous tissue overlying the target vertebra were infiltrated with 1% lidocaine and the periosteum of the pedicles with 0.25% bupivacaine[1]. Patients then received their assigned treatment. Vertebroplasty was performed according to the established standards. For the control group, verbal and physical cues such as pressure on the patient's back were given and the polymethylmethacrylate (PMMA) cement was opened to simulate the odor associated with mixing of PMMA, but the needle was not placed and PMMA was not injected.

Patients in this study were allowed to cross over to the other arm of the study one month after the intervention if adequate pain relief was not achieved but specific numerical thresholds of outcome measures were not used as a limit to cross over. Patients were seen in clinic by a vertebroplasty practitioner one month after the intervention to discuss whether to cross over and receive the alternative therapy. Patients were analyzed according to their originally assigned treatment arms.

The primary outcome measures were scores on back pain (on a scale from 0 to 10) and RDQ at one month. Secondary outcomes of the study included scores for the pain frequency index, pain bothersome index, SOF-ADL, EQ-5D, SF-36 PCS and MCS, and opioids use. Patients were also asked before discharge on the day of the procedure and at each follow-up assessment to guess which procedure they had undergone and to rate their confidence on their guess on a scale from 0 (no confidence) to 10 (complete confidence).

One patient in the vertebroplasty group and two patients in the control group crossed over to the other group before one month. At 3 months, 27 (43%) patients in the control intervention group and 8 (12%) in vertebroplasty group had crossed over to the other arm and received the alternative procedure ($P < .001$). Patients who crossed over to the other arm, regardless of the original assignment, did not achieve the same level of improvement at 3 months as did patients who did not cross over.

Analysis of the results at one month (before cross over) showed no significant differences between the two groups with respect to the primary or secondary outcomes (Tables 4 and 5). The observed differences in pain between the two groups were smaller than minimal clinically important difference (MCID of 1.5). In addition, the proportion of patients who had clinically meaningful improvement in physical disability related to back pain at 1 month did not differ between the two groups (vertebroplasty 40%, control 41%, $P = .99$). Although, there was a higher rate of clinically meaningful improvement in pain (pain reduction of 30% or more) in the vertebroplasty group (64%) than the control group (48%) this was not significant ($P = .06$).

At 14 days, more patients in the control group (63%) correctly guessed their assigned treatment arm compared to the vertebroplasty group (51%). The degree of confidence of their guess was moderate.

The Australian trial was a randomized, parallel group, placebo-controlled trial. Patients were enrolled from April 2004 to October 2008 and the study planned for a 2-year follow-up which will conclude in October 2010. There were four participating sites and patients were recruited from the practices of general

[1] Bupivacaine is a local anesthetic that blocks the generation and the conduction of nerve impulses. The half-life of bupivacaine in adults is 3.5 ± 2 hours

practitioners and specialists and from hospital inpatient and emergency departments.

The inclusion criteria were:

- Back pain for no more than 12 months
- 1-2 painful osteoporotic VCF confirmed by thoracic and lumbar spine radiograph and MRI

The exclusion criteria were:

- Presence of malignant disease in the spine
- Neurological complications
- Osteoporotic vertebral collapse of > 90%
- Fracture through or destruction of posterior wall
- Retropulsed bony fragment or bony fragments impinging on the spinal cord
- Discitis
- Osteomyelitis
- Uncontrolled sepsis
- Non-correctable coagulation disorder
- Medical conditions that make the patient ineligible for emergency decompressive surgery
- Current malignancy
- Dementia
- Previous vertebroplasty
- Inability to give informed consent
- Likelihood of non-compliance with follow-up

The primary end point of the study was the score for overall pain at 3 months. It was calculated that a sample of 24 patients in each arm would give the study 80% power to show at least a 2.5 point (SD of 3) difference in pain scores, based on a two-sided type 1 error of 0.05. A total of 468 participants were considered for inclusion. Two hundred and forty eight (53%) did not meet inclusion criteria, 141 (30%) of potentially eligible patients declined to participate in the study, and one patient died before randomization. As a result, only 78 were included in the study and underwent randomization. However, this sample provided more than 80% power for the primary outcome of the study.

The authors indicated that one factor that may have had influence on the low participation rate was that vertebroplasty became approved for funding in November 2005 therefore promoting the perception that vertebroplasty was already considered an effective procedure by the authorities.

In this study, patients with back pain due to one or two recent VCF (s), confirmed by MRI, were included. The presence of back pain was less than 12 months. However, only two patients in each group had symptoms for longer than 6 months. Patients, investigators, and outcome assessors were all blinded to the treatment assignment.

Vertebroplasty was performed according to a standardized protocol. For patients in the control group, a sham procedure simulating vertebroplasty was used. However, no anesthetic agent was used in the periosteum for immediate pain relief. To simulate vertebroplasty, the vertebral body was gently tapped and PMMA cement was prepared so that the smell permeates the room making the patient to believe he/she is receiving the real procedure. After the intervention, all patients received usual care. Treatment decisions were made at the direction of treating physician, who received up to date guidelines on the management of osteoporosis. Analgesia was given according to standard practice.

Patients included in this study had similar baseline characteristics. The results of this trial showed no significant differences in the primary outcome of overall pain at 1 week, 1 month, 3 months, and 6 months between patients who received vertebroplasty and those who received a sham procedure. There

were also no significant between group differences for any other outcomes, except the QULEFFO scores at 1 week that favoured the sham group. The observed differences between groups at all time points were smaller than minimal clinically important difference (MCID of 1.5 points).

Technical Characteristics of the Studies

All the vertebroplasty procedures in these RCTs were performed by experienced interventionists with adequate training and experience and according to the standard guidelines. Plain x-ray and/or MR imaging techniques were used to determine the characteristics of the fractures (Table 3).

Table 3. Technical Characteristics: Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

	Pre-procedural Imaging Method	Skills of the Operator Performing vertebroplasty	Approach for Vertebroplasty
Kallmes et al. 2009(7)	Either plain film x-ray, MRI or bone scan for all patients	Highly experienced interventionists, having performed a mean of approximately 250 procedures (range, 50-800)	Unipedicular
Buchbinder et al. 2009(8)	MRI for all patients	Experienced interventional radiologists with formal training in PV procedure and appropriate certification. Interventionists were actively performing PV procedures	Unipedicular approach was used and satisfactory infiltration of the vertebral body was confirmed radiographically. A bilateral approach was used only if there was inadequate instillation of cement with unilateral approach
Rousing et al. 2009(9) & 2010 (13)	X-ray for all patients. MRI if > 1 fracture to determine the age of the fracture	Orthopaedic surgeon specialized in spine surgery	Unipedicular or bipedicular
Voormolen et al. 2007(10)	x-ray and MRI for all patients		Bipedicular approach in most cases

Results

Pain Outcomes

Pain was the main or one of the primary outcomes of all these RCTs. It was measured on a scale from 0 to 10, with higher scores indicating more severe pain. The baseline mean pain scores were above 7 points in all studies (vertebroplasty group, 7.1 to 7.4 and control intervention group, 7.1 to 8.8). Two unblinded studies reported an immediate and substantial improvement in back pain scores after vertebroplasty. Voormolen et al. (10) reported that one day after vertebroplasty, the mean scores for pain decreased 2.4 points while it only decreased 0.5 point in patients in control intervention group. The difference in pain scores between the two groups at 1 day after the intervention was statistically significant (Mean difference 2.4, 95% CI -3.7 to -1). Analgesic use compared with pre-treatment values decreased nearly 1 point in vertebroplasty group but increased nearly 1 point in the control intervention group. In another unblinded study, Rousing et al. (9) showed a significant reduction in pain 12 to 24 hours after vertebroplasty (from 7.7 to 2, P = .00).

Studies reported that reduction in pain following vertebroplasty was sustained over time. However, they also found that pain diminished in the control intervention group as well and the difference between the two groups did not reach statistical significance a few days after (Table 4).

Buchbinder et al. (8) reported pain at rest and pain in bed at night. None of the measures differed between these two groups at any time points.

Table 4. Mean Pain Scores After Intervention: Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Study	Baseline Mean±SD	Within the first week	2 weeks	1 month	3 months	6 months	12 months
Liu et al. 2010(11)	PV: 7.9±0.7 BK: 8±0.8 Not significant	**3 days:** PV: 2.3±0.5 BK: 2.6±0.6 Not significant	-	-	-	PV: 2.6±0.6 BK: 2.6±0.6 Not significant	-
Kallmes et al. 2009(7)	PV: 6.9±2 CI: 7.2±1.8 Not significant	**3 days:** PV: 4.2±2.8 CI: 3.9±2.9 Treatment effect: -0.4 (-1.5 to 0.5); P = .37	PV: 4.3±2.9 CI: 4.5±2.8 Treatment effect: 0.1 (-0.8 to 1.1); P = .77	PV: 3.9±2.9 CI: 4.6±3 Treatment effect: 0.7 (-3 to 1.7; P=0.19	-	-	-
Buchbinder et al. 2009(8)	PV: 7.4±2.1 CI: 7.1±2.3 Not significant	**1 week Change:** PV: 1.5±2.5 CI: 2.1±2.8 Diff* -0.7 (-1.8 to 0.4)	-	**Change:** PV: 2.3±2.6 CI: 1.7±3.3 Diff* 0.5 (-0.8 to 1.7)	**Change:** PV: 2.6±2.9 CI: 1.9±3.3 Diff* 0.6 (-0.7 to 1.8)	**Change:** PV: 2.4±3.3 CI: 2.1±3.3 Diff* 0.1 (-1.2 to 1.4)	-
Rousing et al. 2009(9) & 2010(13)	Mean (95% CI) PV: 7.5 (6.6-8.4) CI: 8.8 (8.2-9.3) P = .02	**1 day:** PV: 2 CI: NR	-	-	Mean (95% CI) PV: 1.8 (0.8-2.8) CI: 2.6 (1.2-4) P = .33	-	PV: 2 (1.1-3) CI: 2.9 (1.6-4.1) P = .29
Voormolen et al. 2007(10) VERTOS trial	Mean (95% CI) PV: 7.1 (5-9) CI: 7.6 (5-10) Not significant	Mean (95% CI) **1 day:** PV: 4.7 (1-8) CI: 7.1 (5-10) Mean difference: -2.4 (-3.7 to -1)	Mean (95% CI) PV: 4.9 (0-10) CI: 6.4 (3-9) Mean difference: -1.5 (-3.2 to 0.2)	-	-	-	-

* Adjusted between group mean difference and 95% CI; SD, Standard deviation, PV, Percutaneous vertebroplasty, CI, Control intervention

Minimal Clinically Important Difference

The difference between pain scores of patients who were randomized to vertebroplasty and those who were randomized to control intervention did not reach the minimal clinically important difference of 1.5 points after two weeks. (Figure 1)

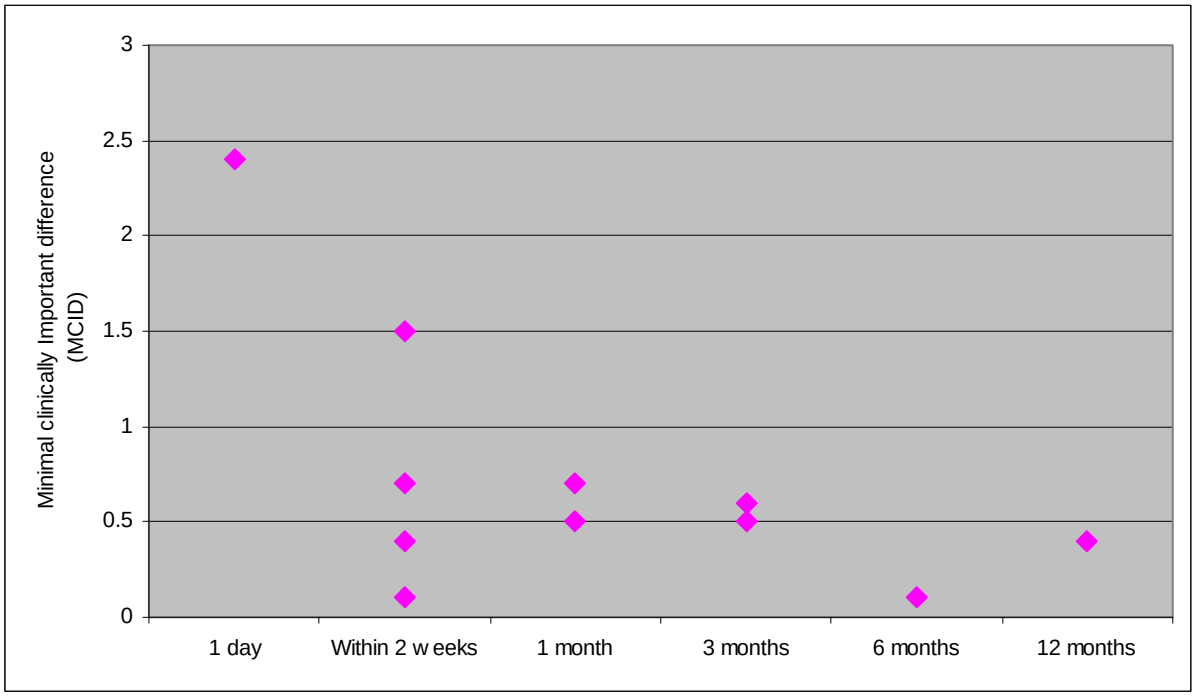

Figure 1. Minimal Clinically Important Difference Between the Pain Scores of the Vertebroplasty and Conservative Group at Various Times

In the Rousing study (9), supplementary assessment of back pain by cross sectional telephone interview performed when all patients (except 3) had completed 12 months follow-up. Patients were asked to answer the question of "How intense was your back pain one month after discharge from the hospital on a scale from 0 to 10". This assessment showed a significant lower pain score in the vertebroplasty group. However, as the authors have indicated, there is a high probability of recall bias to determine the severity of pain months after that experience, although recall should not be different between the groups. In this study, a small number of patients still experienced pain over 5 points after 3 months; 5 in control intervention and 3 in vertebroplasty.

Use of Pain Medications

Voormolen et al. in their open trial (10) reported that analgesic use increased by 0.9 points in patients in control intervention arm and decreased by 0.7 point in patients in vertebroplasty arm at two week follow-up (Mean difference 1.5, 95% CI, -2.3 to -0.08). However, studies with one month follow-up showed no difference in the amount of opioids use. Kallmes et al. in their blinded trial (7) reported no significant differences in opioids use between the two arms of the study at one month after the intervention.

In the study by Buchbinder et al. (8) the amount of opioids use decreased over time in both groups, with

no significant differences between the two groups at any time point. At 1 week, 3 patients in vertebroplasty and 7 patients in control intervention group had stopped taking opioids. At 1 month, 4 patients in vertebroplasty versus 9 in control intervention group, at 3 months 11 in each group, and at 6 months, 17 in vertebroplasty versus 18 in control intervention group had stopped taking opioids. (Figure 2)

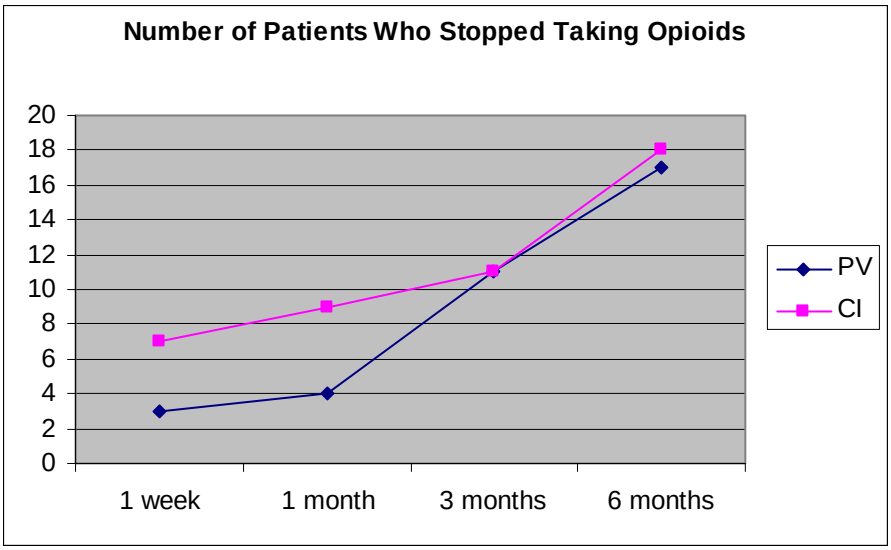

Figure 2. Number of Patients who Stopped Taking Opioids: Buchbinder et al. 2009 (8)

Physical, Mental, and Social Functioning

Studies used two or more of the following scales to measure other aspects of life including physical functioning, mental functioning, and social functioning. A brief description of these scales is provided in the glossary of the scales below Table 5.

Roland-Morris Disability Questionnaire (RDQ)
European Quality of Life-5 Dimensions (ED-5Q)
SF-36 (PCS and MCS)
QUALEFFO
Assessment of quality of Life (AQoL)
Study of Osteoporotic Fracture-Activities of Daily Living (SOF-ADL) scale
Dallas Pain questionnaire (DPQ)
Barthel Index
MMSE

None of the studies found any significant differences between the vertebroplasty group and the control intervention group in any of these measures, with a few exceptions:

- Buchbinder et al. (8) reported a significantly better outcome in QUALEFFO scale for control intervention group at 1 week.
- Rousing et al. (9) reported a significantly better outcome in DPQ for control intervention group at

3 months.

- Rousing et al. (9) reported a significantly better outcome in EQ-5D for vertebroplasty but did not consider this difference to be significant because of the difference in baseline values.
- Voormolen et al. (10) reported significantly better outcomes in RDQ and QUALEFFO for vertebroplasty at 2 weeks.

Table 5 summarizes the scores obtained through the use of different scales measured at different time points.

Table 5. Changes in Physical, Mental, and Social Functioning: Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Study	RDQ Mean±SD	EQ-5D Mean±SD	SF-36 Mean±SD	AQoL Mean±SD	QUALEFFO Mean±SD	Other Scales Mean±SD
Kallmes et al. 2009(7)	(PO) Baseline: PV: 16.6±3.8 CI: 17.5±4.1 3 days: PV: 13±5.2 CI: 12.5±5.5 Treatment effect, -0.9 (-2.7 to 0.8) P = .3 14 days: PV: 12.4±5.8 CI: 12.3±5.9 Treatment effect, -0.6 (-2.4 to 1.2) P = .35 1 month; PV: 12±6.3 CI: 13±6.4 Treatment effect, 0.7 (95% CI, -1.3 to 2.8) P=0.49	Baseline: PV: 0.57±0.18 CI: 0.54±0.23 1 month: PV: 0.7±0.18 CI: 0.64±0.2 Treatment effect, 0.05 (-0.01 to 0.11) P = .13	SF-36 (PCS) Baseline: PV: 25.3±7.8 CI: 25.3±7.3 1 month: PV: 29.7±9.6 CI: 28.7±8 Treatment effect, 1 (-1.7 to 3.7) P = .45 SF-36 (MCS) Baseline: PV: 44.8±11.8 CI: 41.5±14.1 1 month: PV: 46.9±12 CI: 45.6±14.8 Treatment effect, 1 (-3.7 to 4.6) P = .83			**1 month:** **SOF-ADL** Baseline: PV: 10±3.6 CI: 10.3±2.8 1 month: PV: 7.7±3.7 CI: 8.2±3.6 Treatment effect, 0.4 (-0.8 to 1.6) P = .51 **Pain frequency index:** Baseline: PV: 3±0.8 CI: 3.1±0.8 1 month: PV: 2.1±1.2 CI: 2.3±1.1 Treatment effect, 0.2 (-0.2 to 0.6) P = .33 **Pain bothersome index:** Baseline: PV: 2.9±0.7 CI: 3.1±0.8 1 month: PV: 1.9±1.1 CI: 2.1±1.1 Treatment effect, 0.2 (-0.2 to 0.6) P = .33
Buchbinder et al. 2009(8)	Baseline: PV: 17.3±2.8 CI: 17.3±2.9 Change at 1 week: PV: 1.8±5 CI: 4±6.8 Diff (95% CI):	Baseline: PV: 0.3±0.32 CI: 0.28±0.33 Changes in 1 week: PV: 0.1±0.3 CI: 0.1±0.3 Diff (95% CI):	-	Baseline: PV: 0.33±0.25 CI: 0.27±0.26 Changes in 1 week: PV: 0±0.2 CI: 0.1±0.3 Diff (95% CI):	Baseline: PV: 56.9±13.4 CI: 59.6±17.1 Changes in 1 week: PV: -0.5±7.4 CI: 3.6±9.2 Diff (95% CI):	

Study	RDQ Mean±SD	EQ-5D Mean±SD	SF-36 Mean±SD	AQoL Mean±SD	QUALEFFO Mean±SD	Other Scales Mean±SD
	-2.1 (-5.2 to 0.9) Changes in 1 month: PV: 4.4±6.6 CI: 3.1±6.8 Diff (95% CI): 1.7 (-1.8 to 5.2) Changes in 3 months: PV: 3.7±5.4 CI: 5.3±7.2 Diff (95% CI): -1.5 (-4.8 to 1.7) Changes in 6 months: PV: 4.1±5.8 CI: 3.7±5.8 Diff (95% CI): 0 (-0.3 to 2.9)	0.0 (-0.1 to 0.2) Changes in 1 month: PV: 0.1±0.3 CI: 0.1±0.3 Diff (95% CI): 0 (-0.1 to 0.1) Changes in 3 months: PV: 0.2±0.3 CI: 0.2±0.4 Diff (95% CI): 0 (-0.1 to 0.2) Changes in 6 months: PV: 0.2±0.4 CI: 0.2±0.4 Diff (95% CI): 0 (-0.1 to 0.2)		0 (-0.1 to 0.1) Changes in 1 month: PV: 0±0.2 CI: 0±0.3 Diff (95% CI): 0 (-0.1 to 0.1) Changes in 3 months: PV: 0±0.2 CI: 0.1±0.3 Diff: 0 (-0.1 to 0.1) Changes in 6 months: PV: 0±0.3 CI: 0.1±0.3 Diff (95% CI): 0.1 (-0.1 to 0.2)	-0.4 (-7.8 to -0.2)† Changes in 1 month: PV: 2.8±9.3 CI: 2.4±12.3 Diff (95% CI): 0.9 (-4.2 to 6) Changes in 3 months: PV: 6±9.6 CI: 6.1±13.7 Diff (95% CI): 0.7 (-4.4 to 5.7) Changes in 6 months: PV: 6.4±13.4 CI: 6.1±13.4 Diff (95% CI): 0.6 (-5.1 to 6.2)	
Rousing et al. 2009(9) & 2010(13)		Mean (95% CI) Baseline: PV: 0.356 (0.196-0.516) CI: 0.083 (-0.151-0.317) 3 months: PV: 0.731 (0.653-0.809) CI: 0.543 (0.387-0.699) P = 0.04*‡ 12 months: PV: 0.675 (0.576-0.775) CI: 0.571 (0.448-0.694) P = .19	Mean (95% CI) **SF-36, PCS** Baseline: PV: 36.7 (30-43.4) CI: 33.4 (26.2-40.7) 3 months: PV: 34 (30.1-37.9) CI: 29.3 (24.5-34.1) P = .12 12 months: PV: 32.1 (27.8-36.3) CI: 30.5 (25.2-35.7) P = .63 **SF-36, MCS** Baseline: PV: 49.7 (43.6-55.8) CI: 49.6 (41.9-53.7) 3 months: PV: 48.9 (43.8-54) CI: 46.2 (39.2-53.2) P = 0.51 12 months: PV: 48.7 (42.7-54.6) CI: 49 (43.9-54.1)			**DPQ** <u>Daily activities:</u> Baseline; PV: 47.8 (22.5 to 73.1) CI: 68.5 (47 to 90.1) 3 months: PV : 47.1 (32.9 to 61.4) CI: 57.4 (40.7 to 74.1) P = .33 12 months: PV: 53 (38.3 to 67.7) CI: 53.6 (34.8 to 72.5) P = .95 <u>Work & leisure:</u> Baseline: PV: 41.1 (20.7 to 61.5) CI: 68.7 (47.8 to 89.6) 3 months: PV: 44.5 (30.4 to 58.7) CI: 65.2 (50.4 to 80.1) P = .04† 12 months: PV: 46.1 (31.4 to 60.9) CI: 49.2 (31.5 to 66.9) P = .78

Study	RDQ Mean±SD	EQ-5D Mean±SD	SF-36 Mean±SD	AQoL Mean±SD	QUALEFFO Mean±SD	Other Scales Mean±SD
			P = .93			<u>Anxiety & depression</u> Baseline: PV: 31.5 (12.6 to 50.4) CI: 43 (19.9 to 66.1) 3 months: PV: 28.7 (15.1 to 42.3) CI: 40 (20.8 to 59.2) P = .3 12 months: PV: 31.3 (16.5 to 46.2) CI: 35.3 (20.4 to 50.2) P = .7 <u>Social interest:</u> Baseline: PV: 23.8 (9.9 to 37.7) CI: 41 (23.3 to 58.7) 3 months: PV: 24.1 (13.2 to 35) CI: 30.7 (15.9 to 45.5) P = .46 12 months: PV: 32.9 (18.9 to 46.9) CI: 30.7 (16.5 to 44.8) P = .82 **Barthel Index** Mean (95% CI) Baseline: PV: 17.7 (15.6-19.8) CI: 17 (14.2-19.8) 3 months: PV: 19.6 (19-20.3) CI: 18.1 (16.8-19.4) P = 0.07 12 months: PV: 19.8 (19.5-20) CI: 18.5 (17.6-19.3) P = .02† **MMSE %** Mean (95% CI) Baseline:

Study	RDQ Mean±SD	EQ-5D Mean±SD	SF-36 Mean±SD	AQoL Mean±SD	QUALEFFO Mean±SD	Other Scales Mean±SD
						PV: 86.8 (81.8-91.8) CI: 86.5 (81.8-91.3) 3 months: PV: 87.2 (79.7-94.7) CI: 90.5 (86.9-94.2) P =.36 12 months: PV: 88.3 (81.2-95.3) CI: 88.7 (80.6-96.8) P = .93
Voormolen et al. 2007(10)	Mean (95% CI) Baseline: PV: 15.7 (8-22) CI: 17.8 (9-24) 2 weeks: PV: 13 (3-22) CI: 18 (9-23) Diff (95% CI): -5, -8.4 to -1.2*				Mean (95% CI) Baseline: PV: 60 (37-86) CI: 67 (38-86) 2 weeks: PV: 53 (28-79) CI: 67 (40-88) Diff (95% CI): -6.1, -10.7 to -1.6*	

* In favour of PV group; † In favour of CI group; ‡ Since the two groups differed significantly at baseline as well, they are not comparative regarding ED5Q;
PO, Primary outcome; PV, Percutaneous vertebroplasty; CI, Control intervention; SD, Standard deviation; CI, Confidence interval; Diff, Mean difference

Glossary for Scales Used in Vertebroplasty Studies

Pain score measured on a scale from 0 to 10 with 0 indicating no pain and 10 indicating maximum imaginable pain. The minimal clinically important difference in scores in population with back pain is 1.5. (14)

Roland-Morris Disability questionnaire (RDQ) is a self-administered disability measure on a scale of 0 to 23, with higher scores indicating greater disability and 2-3 points representing the minimal clinically important difference. (15)

European Quality of Life-5 Dimensions (ED-5Q) is an instrument that measures health outcome and consists of 5 dimensions: Mobility, self care, usual activities, pain, and psychological distress; scores range from 0 to 1, with 1 indicating perfect health and 0.074 representing the minimal clinically important difference. (16)

SF-36 is a generic 36-item questionnaire compiled from the Rand Health Insurance Long Form Health Status Scale. The survey consists of 36 questions covering 8 dimensions: Physical function, social function, role physical, role emotional, mental health, vitality, bodily pain, and general health. Each dimension is scored on a weighted 0-100 scale and the overall score is calculated. MCID for SF-36 (PCS) in patients who underwent lumbar spine surgery was 4.9. (17)

Quality of Life Questionnaire on the European Foundation for Osteoporosis (QUALEFFO) is a 41-item vertebral-fracture specific and osteoporosis specific questionnaire in which scores range from 0 to 100, with lower scores indicating a better quality of life. (18)

Assessment of quality of Life (AQoL) questionnaire is sensitive to changes in frail elderly in which scores ranges from -0.04 to 1, with 1 indicating perfect health and 0.06 representing the minimal clinically important difference. (19)

Study of Osteoporotic Fracture-Activities of Daily Living (SOF-ADL) scale range from 0 to 18, with higher scores indicating more back related disability

Dallas Pain questionnaire (DPQ) is a 16-item visual analogue scale evaluating the affection of chronic pain on 4 aspects of life: Daily activities, work and leisure, anxiety and depression, and social interest; lower scores indicating better outcome

Barthel index is a ten-item scale that measure daily functions: Feeding, bathing, grooming, dressing, bowel, bladder, toilet use, transfers, mobility, and stairs. From these topics, a sum score is calculated (0= worse condition, 20= best condition)

Mini Mental State Examination (MMSE) is a quantitative measurement of cognitive status in adults. It includes orientation, registration, attention, calculation, recall, and language (0=worse cognitive condition, 30=best cognitive condition)

Physical Tests

Rousing et al. (9) performed 3 physical tests on the patients before and at different time points after the intervention. Physical tests included tandem test (balance test), UP & Go test, and the repeated chair test (muscle power test). The tandem test is an indicator of immediate balance measured. The patients stand in 3 different and increasingly demanding positions and time (in seconds) are recorded. The UP & GO test quantifies functional mobility and measures the time in seconds required to rise from a standard arm

chair, walk 3 meter, turn around, return to the chair, and sit down again. In the repeated chair test, the patient performs repeated chair stands for 30 seconds. In Rousing study (9), none of these measures were different between the two groups at 3 and 12 months follow-ups.

Results of Cross Over

In the INVEST trial, patients in the control intervention arm who crossed over to the vertebroplasty arm had some early improvement in pain after the procedure but this improvement had disappeared by 1 month. Patients in the vertebroplasty arm who crossed over to the control intervention arm had higher levels of pain and disability at 3 days and 14 days after vertebroplasty as compared with those who did not cross over. However, analysis of 3 months follow-up data showed that in either group, crossing over to the other arm did not result in the same level of improvement seen in those who did not cross over. (Figure 3)

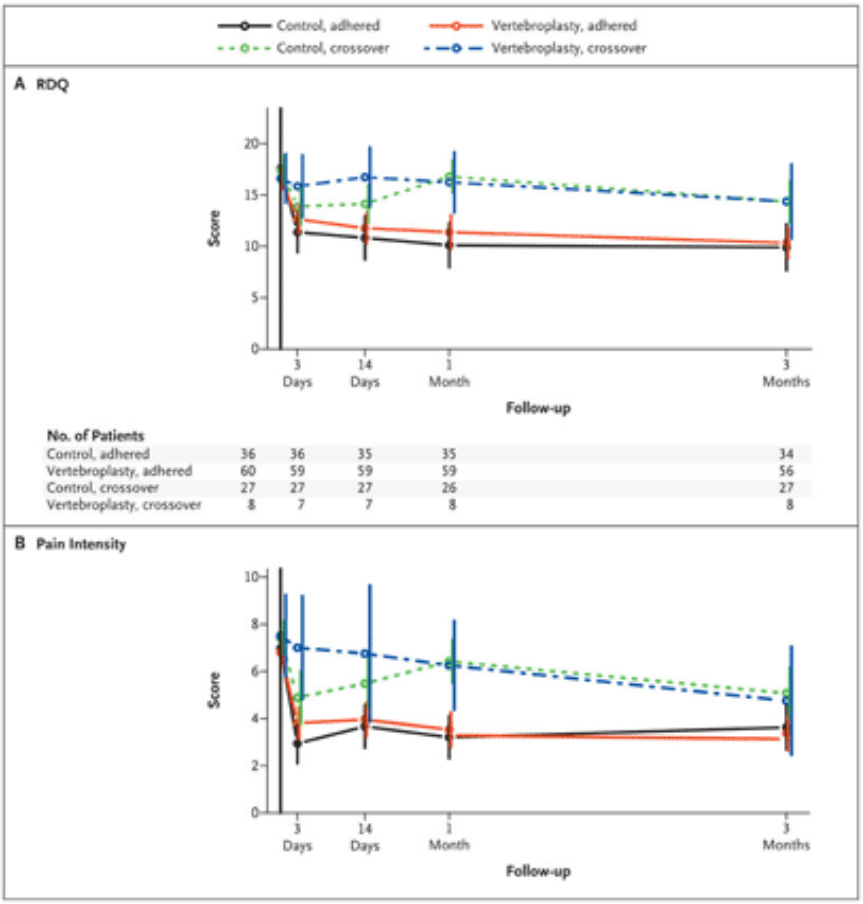

Figure 3. Scores on Measures of Disability and Pain Over a 3–Month Period

Source: *A randomized trial of vertebroplasty for osteoporotic spinal fractures**;** Kallmes,D.F.; Comstock,B.A.; Heagerty,P.J.; Turner,J.A.; Wilson,D.J.; Diamond,T.H.; Edwards,R.; Gray,L.A.; Stout,L.; Owen,S.; Hollingworth,W.; Ghdoke,B.; nnesley-Williams,D.J.; Ralston,S.H.; Jarvik,J.G; New England Journal of Medicine; 361 (6) 569-579*

The black vertical lines indicate the time when baseline measures were taken
The colored vertical lines represent 95% confidence interval

Safety of Vertebroplasty

Generally, about 20% of patients with a history of osteoporotic VCF will experience a new VCF within a year depending on the severity of the prior fracture. (13) However, women with pre-existing VCFs have a 4-time increased risk of subsequent vertebral fracture. (20)

The rate of adverse events and incidence of new fractures are shown in Table 6.

Table 6. Incidence of New Vertebral Fractures and Adverse Events: Randomized controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Study	New Vertebral Fracture N	Adverse Events N
Liu et al. 2010	Within 2 months PV: 0 BK: 2 adjacent	NR
Kallmes et al. 2009(7)	NR	PV: 1 injury to the thecal sac during The procedure which required hospitalization CI: 1 tachycardia
Buchbinder et al. 2009(8)	Within 6 months: PV: 3 CI: 4	Chest pain: PV: 3 CI: 0 Pain or burning in thigh or leg: PV: 4 CI: 2 Increased pain or muscle cramping around puncture site: PV: 2 CI: 1 Minimal leakage reported in 14 (37%) Osteomyelitis in a patients who did not receive cephalothin due to multiple drug allergies
Rousing et al. 2009(9) & 2010(13)	Within 3 months: PV: 3; 2 were adjacent CI: 1; not adjacent RR for all new VCFs, 2.9 (95% CI, 0.3-25.7) After 3 months and up to 12 months: PV: 4; 1 adjacent CI: 3, non adjacent RR for all new VCFs after 12 months, 1.3	Extravertebral cement leakages following PV
Voormolen et al. 2007(10)	PV: 2 adjacent VCF CI: 0	PV: 1 pedicle chip due to PV (but crossed over from CI)

PV, Percutaneous vertebroplasty; CI, Control intervention

Quality of the Studies

Jadad instrument (4) was used to assess the quality of RCTs. The items in this instrument were presented as questions to elicit "Yes" or "No" answers. A numerical score from 0 to 5 is assigned with 0 being the lowest and 5 being the highest quality of the study. Jadad instrument was used to determine the quality of the RCTS on vertebroplasty in terms of how they were designed and how they were conducted (Table 7).

Table 7. Jadad Score Calculation: Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures (4)

Item	Kallmes et al. 2009(7)	Buchbinder et al. 2009(8)	Rousing et al. 2009(9) & 2010(13)	Voormolen et al. 2007(10)
Was the study described as randomized (this includes such words as "randomly", "random", and "randomization")?	Yes	Yes	Yes	Yes
Was the method used to generate the sequence of randomization described and was it appropriate (e.g., table of random numbers, computer-generated)?	Yes Eligible patients were randomly assigned in blocks of 4 to 12, according to the enrollment site, with the use of a random-number generator in data coordinating centere. The assignments were then placed in numbered, opaque, sealed envelopes, with a series of envelopes for each study centre. The assignments were revealed to the clinicians in the procedure room after the patients was sedated and received local anesthesia. The baseline characteristics of the patients in the two arms were the same.	Yes Eligible patients were randomly assigned in blocks of 4 and 6, according to computer-generated random numbers, to undergo PV or sham procedure. The baseline characteristics of the patients in the two arms were the same.	Yes Sealed envelopes were prepared beforehand and were sorted randomly. The baseline characteristics of the patients in the two arms were the same.	Yes Randomization was done by independent central operator. The baseline characteristics of the patients in the two arms were the same.
Was the study described as double-blind?	Yes The protocol specified that study group assignments should be concealed from all patients and study personnel who performed follow-up assessments for the duration of the study.	Yes Patients, investigators, and outcome assessors were blinded to the assignment.	No	No
Was the method of double-blinding described and was it appropriate (e.g., identical placebo, active placebo, dummy)?	Yes For control group, verbal and physical cues such as pressure on the patient's back were given and the PMMA cement was opened to simulate the odor associated with mixing of PMMA, but the needle was not placed and	Yes After needle placement in the sham group the vertebral body was gently tapped to simulate PV procedure and the PMMA cement was prepared so that it	No	No

Item	Kallmes et al. 2009(7)	Buchbinder et al. 2009(8)	Rousing et al. 2009(9) & 2010(13)	Voormolen et al. 2007(10)
	PMMA was not injected.	smell permeate the room making the patient to believe she/he is receiving the real procedure.		
Was there a description of withdrawals and dropouts?	Yes Consort chart for the study was published.	Yes Consort chart for the study was published.	Yes Consort chart for the study was published.	Yes Consort chart for the study was published.
Deduct 1 point if the method used to generate the sequence of randomization was described but was inappropriate (e.g., patients were allocated alternately or according to date of birth or hospital number).	N/A	N/A	N/A	N/A
Deduct 1 point if the study was described as double-blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	N/A	N/A	N/A	N/A

The numerical values for the two blinded RCTs were 5/5 and these two studies were considered as "high quality". The numerical values for the two open RCTs were 3/5 and these two were considered as "moderate quality".

Vertebroplasty Versus Balloon Kyphoplasty

Liu et al. (11) conducted a randomized clinical trial to investigate the effectiveness of vertebroplasty versus balloon kyphoplasty. One hundred patients with osteoporotic VCFs at the thoracolumbar (T12-L1) vertebra were randomly assigned into two groups: vertebroplasty (50) and kyphoplasty (50). Block randomization technique was used. The mean age of the patients was 74.3±6.4 (range, 57-88) in the vertebroplasty group and 72.3±7.6 (range, 57-84) in kyphoplasty group. Both procedures were performed within 43 days after injury (acute and subacute fractures). The mean duration between injury and surgery was 15.8±6.7 for vertebroplasty and 17±7.7 for balloon kyphoplasty. Patients in the two groups did not differ significantly in age, gender, location of VCFs, duration between injury and surgery, pre-operative pain scores, vertebral body height, or kyphotic wedge angle.

Measurements of pain on a 10-point visual analogue scale, and kyphotic wedge angle (to evaluate kyphosis) were made before and after surgery. The minimum follow-up period was 6 months.

The operation time for the kyphoplasty group was longer than the vertebroplasty group (46.2±4.5 vs 44±4.4 min, P < .05). The amount of injected PMMA was also greater in kyphoplasty than vertebroplasty (5.56±0.62 ml, vs 4.91±0.65 ml, P < .001). Two patients in the kyphoplasty group developed new adjacent VCFs; one at 41 days and one at 50 days after the procedure.

The pain score for kyphoplasty decreased from 8±0.8 to 2.6±0.6 at 3 days after surgery (P < .001) and remained constant until the final follow-up at 6 months. Similarly, the pain score in the vertebroplasty group decreased from 7.9±0.7 to 2.3±0.5 at 3 days (P < .001) and it was 2.6±0.6 at 6 months follow-up. The study did not find any statistical significance difference between the two treatment groups at any time period examined.

In the kyphoplasty group, the vertebral body height increased from 1.13±0.34 cm to 2.04±0.41 cm (P < .001). In the vertebroplasty group, this measure increased from 1.01±0.22 cm to 1.32±0.26 cm (P < .001). The post operative kyphotic wedge angle in the kyphoplasty group was 9±5.7 and it was 12.2±3.6 in the vertebroplasty group (P < .001).

Kyphoplasty and vertebroplasty resulted in significant increase in vertebral body height and significant reduction in kyphotic wedge angle. However, these measures were both significantly greater with kyphoplasty compared to vertebroplasty (P < .001) (Table 8).

Table 8. Vertebral Body Height and Kyphotic Wedge Angle: Balloon Kyphoplasty Versus Vertebroplasty

Procedure	Vertebral Body Height cm	Kyphotic Wedge Angle Degree	P-value
Balloon kyphoplasty	Baseline: 1.13±0.34 After: 2.04±0.41 P < .001	Baseline: 17±7.3 After: 9±5.7 P < .001	P < .001*
Vertebroplasty	Baseline: 1.01±0.22 After: 1.32±0.26 P < .001	Baseline: 15.5±4.2 After: 12.2±3.6 P < .001	P < .001*

* In favor of balloon kyphoplasty

Summary and Conclusion

Two blinded RCTs on vertebroplasty provide the highest level of evidence available to date. Results of these two trials are supported by findings of an open randomized trial with 12 months follow-up

Blinded RCTs showed:

- No significant differences in pain scores of patients who received vertebroplasty and patients who received a sham procedure as measured at 3 days, 2 weeks and 1 month in one study and at 1 week, 1 month, 3 months, and 6 months in the other.
- The observed differences in pain scores between the two groups were neither statistically significant nor clinically important at any time points.
- The above findings were consistent with the findings of an open RCT in which patients were followed for 12 months. This study showed that improvement in pain was similar between the two groups at 3 months and were sustained to 12 months.
- In the blinded RCTs, physical, mental, and social functioning were measured at the above time points using 4-5 of the following 7 instruments: RDQ, EQ-5D, SF-36 PCS, SF-36 MCS, AQoL, QUALEFFO, SOF-ADL.
- There were no significant differences in any of these measures between patients who received vertebroplasty and patients who received a sham procedure at any of the above time points (with a few exceptions in favour of control intervention).
- These findings were also consistent with the findings of an open RCT which demonstrated no significant between group differences in scores of ED-5Q, SF-36 PCS, SF 36 MCS, DPQ, Barthel, and MMSE which measure physical, mental, and social functioning (with a few exceptions in favour of control intervention).
- One small (n=34) open RCT with a two week follow-up detected a significantly higher improvement in pain scores at 1 day after the intervention in vertebroplasty group compared with conservative treatment group. However, at 2 weeks follow-up, this difference was smaller and was not statistically significant.
- Conservative treatment was associated with fewer clinically important complications.
- Risk of new VCFs following vertebroplasty was higher than those in conservative treatment but it requires further investigation.

Economic Analysis

Ontario Perspective

Volumes and costs in Ontario were accessed on May 2010 from the Ministry of Health and Long-Term Care (MOHLTC) Health Analytics Branch for the following fee codes of vertebroplasty and kyphoplasty:

N570 Vertebroplasty (injection of bone cement) as sole procedure, first level
E388 Vertebroplasty combined with any other procedure, first level, to other procedure
E391 Vertebroplasty, each additional level, to N570 or E388
E381 Intra-operative, diagnostic or physiological neuro monitoring, to N570 or E388
N583 Kyphoplasty (balloon tamp and injection of bone cement) as sole procedure, first level
E392 Kyphoplasty combined with any other procedure, first level, to other procedure
E393 Kyphoplasty, each additional level, to N583 or E392
E381 Intra-operative, diagnostic or physiological neuro monitoring, to N583 or E392

The fee codes were obtained from Ontario Schedule of Benefits (OSB) for Physician Fees (21) accessed May 2010. Figure 4 describes the expenditure associated with both vertebroplasty and kyphoplasty in Fiscal Years (FY) 2005-2008. The expenditure cost included the professional, anesthesia and surgical assistance fees.

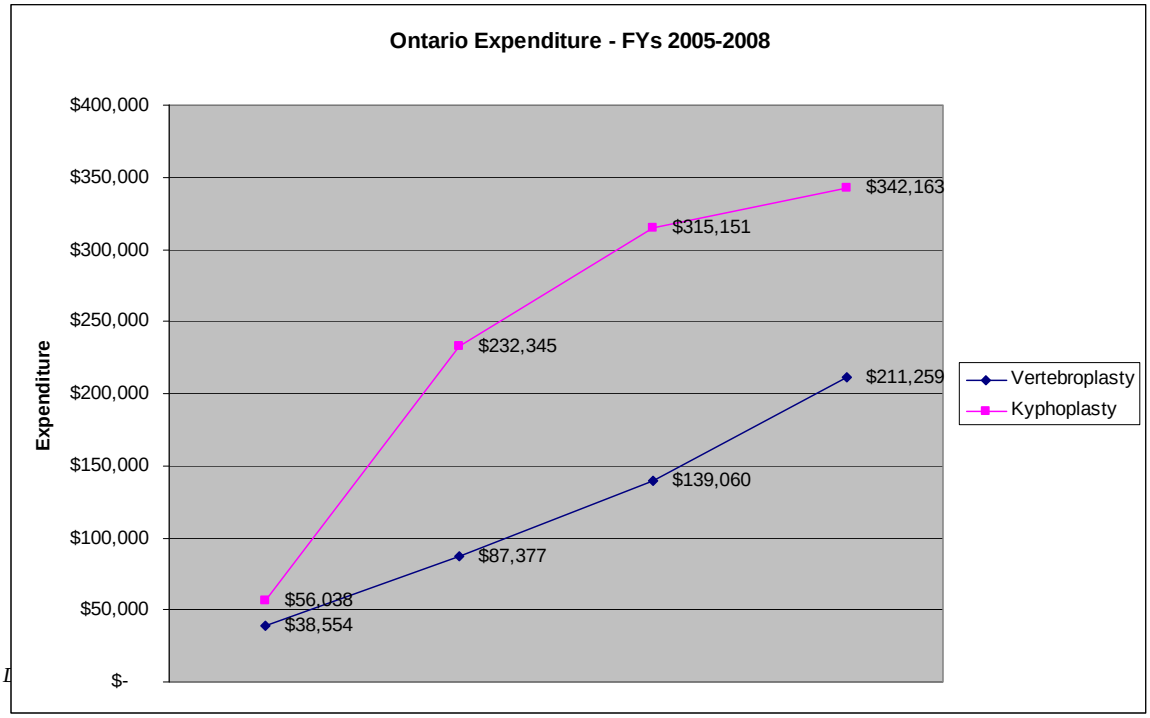

Figure 4. Ontario expenditure for vertebroplasty and kyphoplasty for FYs 2005-2008.

Conventional therapy in this patient population with osteoporotic vertebral compression fracture traditionally consists of pharmacotherapy of analgesic opiate agonists or non-steroidal anti-inflammatory agents. A typical dose from the Compendium of Pharmaceuticals and Specialties (22) (CPS) for Tylenol 3 would be 1-2 tablets every 4 hours PRN, not exceeding 12 tablets a day for 2-4 weeks. A typical dose

for Naprosyn from the CPS (22) would be 2 tablets a day for 2-4 weeks. At $0.0524/tablet from the Ontario Drug Benefit (ODB) Formulary (23), Tylenol 3 would cost $17.61/month/person. At $0.2110/tablet from the ODB (23), Naprosyn would cost $11.82/month/person.

Appendix 3 describes the number of physicians, patients and services and fee paid for each service obtained from MOHLTC.

Glossary

MCID	Minimal clinically important difference reflects the smallest difference in score which is clinically meaningful and important enough to change patient management.
Open trial	A randomized trial in which no one is blinded to group assignment
Parallel design trial	A trial in which the treatment and the control is applied to two separate groups of patients but in contrast to the cross over design, the groups remain in their assigned treatment arms
Placebo	A placebo is an inactive and generally harmless substance or a procedure without specific influence on the condition being treated. A placebo is given to the patient in place of a real medication. Although it is an inert substance or inactive procedure and has no physiological effect on the patient's specific condition, it may have a psychological effect that arises from patient's expectations concerning receiving the treatment rather than from the treatment itself. Placebos are used in controlled experiments to test the efficacy of another substance
Placebo effect	The therapeutic effect produced by placebo
Sham	Simulated medical intervention, a placebo

Appendices

Appendix 1: Literature Search Strategies

Search date: August 9, 2010
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, Centre for Reviews and Dissemination/International Agency for Health Technology Assessment

Database: Ovid MEDLINE(R) <1996 to July Week 4 2010>
Search Strategy:
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1 exp Balloon Dilatation/ or exp Vertebroplasty/ (35665)
2 (kyphoplasty or vertebroplasty).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (1552)
3 1 or 2 (36642)
4 exp Spinal Fractures/ (6142)
5 exp Fractures, Compression/ (562)
6 ((spinal or spine or vertebr* or compression) adj2 fracture*).ti,ab. (5622)
7 exp Osteoporosis/ (23641)
8 osteoporo*.ti,ab. (26669)
9 or/4-8 (37889)
10 3 and 9 (1217)
11 limit 10 to (english language and humans and yr="2005 -Current") (709)
12 limit 11 to (controlled clinical trial or meta analysis or randomized controlled trial) (29)
13 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (42417)
14 (health technology adj2 assess$).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (901)
15 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (84725)
16 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (450663)
17 exp Double-Blind Method/ (61218)
18 exp Control Groups/ (916)
19 exp Placebos/ (10880)
20 (RCT or placebo? or sham?).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (111574)
21 or/12-20 (581211)
22 11 and 21 (97)

Database: EMBASE <1980 to 2010 Week 31>
Search Strategy:
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1 exp kyphoplasty/ or exp percutaneous vertebroplasty/ (2098)
2 exp balloon dilatation/ (8973)
3 (kyphoplasty or vertebroplasty).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (2522)
4 1 or 2 or 3 (11481)
5 vertebra fracture/ or exp spine fracture/ (14431)
6 ((spinal or spine or vertebr* or compression) adj2 fracture*).ti,ab. (10243)
7 exp OSTEOPOROSIS/ (63495)
8 osteoporo*.ti,ab. (48519)
9 or/5-8 (84612)
10 4 and 9 (1850)
11 limit 10 to (human and english language and yr="2005 -Current") (1023)
12 Randomized Controlled Trial/ (266254)
13 exp Randomization/ (51020)
14 exp RANDOM SAMPLE/ (2352)
15 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (443856)
16 (health technology adj2 assess$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (1270)
17 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (110076)
18 Double Blind Procedure/ (94970)
19 exp Triple Blind Procedure/ (15)
20 exp Control Group/ (14259)
21 exp PLACEBO/ or placebo$.mp. or sham$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (286219)
22 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (668299)
23 (control$ adj2 clinical trial$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (400267)
24 or/12-23 (1166966)
25 11 and 24 (179)

Appendix 2: GRADE of Evidence

GRADE Table for Randomized Controlled Trials of Percutaneous Vertebroplasty for Treatment of Osteoporotic Vertebral Fractures

Population	*Outcome*	*Number of studies*	*Study Design*	*Quality of Studies*	*Consistency*	*Directness*	*Other Modifying Factors*	*Grade*
Patients with osteoporotic VCF	Back pain due to VCF	2 • Kallmes et al. 2009(7) • Buchbinder et al. 2009(8)	RCT=High	High	High	No uncertainty	N/A	High
Patients with osteoporotic VCF	Back pain due to VCF	2 • Rousing et al. 2009(9) • Voormolen et al. 2007(10)	RCT=High	Moderate	High	No uncertainty	N/A	Moderate

Appendix 3: Fee for Service Volume and Cost Fiscal Year 2005-2008

Fiscal Year 2005 - ***Service Date from April 1, 2005 to March 31, 2006, Assessed from April 1, 2005 to September 30, 2006 (M7)***						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
N570A	Professional	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	15	53	57	$24,786.00
N570C	Anaesthesia	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	18	19	575	$6,905.75
E388A	Professional	VERTEBROPLSTY COMBINED WITH ANY OTHR PROCEDURE,1ST LEVEL,AD	less than 5	less than 5	less than 5	$612.00
E391A	Professional	VERTEBROPLASTY, EACH ADDITIONAL LEVEL, ADD	12	23	28	$5,712.00
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	less than 5	less than 5	less than 5	$537.90
TOTAL					**660**	**$38,553.65**
N583A	Professional	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	9	36	36	$34,854.80
N583B	Surgical Assist	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	less than 5	14	268	$2,787.20
N583C	Anaesthesia	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	16	27	765	$9,187.65
E392A	Professional	KYPHOPLASTY COMBINED WITH ANY OTHER PROCEDURE,1ST LEVEL, AD	less than 5	less than 5	less than 5	$1,530.00
E393A	Professional	KYPHOPLASTY, EACH ADDITIONAL LEVEL, ADD	less than 5	9	14	$7,140.00
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	less than 5	less than 5	less than 5	$537.90
TOTAL					**1,083**	**$56,037.55**

Fiscal Year 2006 - ***Service Date from April 1, 2006 to March 31, 2007, Assessed from April 1, 2006 to September 30, 2007 (M7)***						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
N570A	Professional	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	18	110	123	$56,133.15
N570B	Surgical	VERTEBROPLASTY(INJECTN	less than 5	less than 5		$426.40

Fiscal Year 2005 - *Service Date from April 1, 2005 to March 31, 2006, Assessed from April 1, 2005 to September 30, 2006 (M7)*						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
	Assist	BONE CEMENT) SOLE PROCEDURE,1ST LEVE			41	
N570C	Anaesthesia	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	27	36	1,205	$14,924.05
E388A	Professional	VERTEBROPLSTY COMBINED WITH ANY OTHR PROCEDURE,1ST LEVEL,AD	7	19	19	$3,876.00
E391A	Professional	VERTEBROPLASTY, EACH ADDITIONAL LEVEL, ADD	16	40	51	$10,404.00
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	less than 5	9	9	$1,613.70
TOTAL					**1,448**	**$87,377.30**
N583A	Professional	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	15	142	148	$142,518.73
N583B	Surgical Assist	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	13	31	673	$6,999.20
N583C	Anaesthesia	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	47	75	2,314	$28,730.64
E392A	Professional	KYPHOPLASTY COMBINED WITH ANY OTHER PROCEDURE,1ST LEVEL, AD	less than 5	16	18	$8,160.00
E393A	Professional	KYPHOPLASTY, EACH ADDITIONAL LEVEL, ADD	7	39	89	$43,273.50
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	6	15	15	$2,662.61
TOTAL					**3,257**	**$232,344.68**

Fiscal Year 2007 - *Service Date from April 1, 2007 to March 31, 2008, Assessed from April 1, 2007 to September 30, 2008 (M7)*						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
N570A	Professional	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	27	171	191	$86,976.68
N570B	Surgical Assist	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	less than 5	5	112	$1,202.80
N570C	Anaesthesia	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	52	70	2,454	$31,314.93

Fiscal Year 2005 - *Service Date from April 1, 2005 to March 31, 2006, Assessed from April 1, 2005 to September 30, 2006 (M7)*						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
E388A	Professional	VERTEBROPLSTY COMBINED WITH ANY OTHR PROCEDURE,1ST LEVEL,AD	11	17	18	$3,672.00
E391A	Professional	VERTEBROPLASTY, EACH ADDITIONAL LEVEL, ADD	15	50	70	$14,280.00
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	5	9	10	$1,613.70
TOTAL					**2,855**	**$139,060.11**
N583A	Professional	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	23	186	206	$197,449.39
N583B	Surgical Assist	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	15	31	663	$7,161.20
N583C	Anaesthesia	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	54	103	3,325	$42,159.31
E392A	Professional	KYPHOPLASTY COMBINED WITH ANY OTHER PROCEDURE,1ST LEVEL, AD	6	22	22	$11,220.00
E393A	Professional	KYPHOPLASTY, EACH ADDITIONAL LEVEL, ADD	13	48	113	$53,754.00
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	7	19	19	$3,406.70
TOTAL					**4,348**	**$315,150.60**

Fiscal Year 2008* - *Service Date from April 1, 2008 to March 31, 2009, Assessed from April 1, 2008 to September 30, 2009 (M7)*						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
N570A	Professional	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	36	257	288	$133,902.03
N570B	Surgical Assist	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	9	19	351	$4,082.75
N570C	Anaesthesia	VERTEBROPLASTY(INJECTN BONE CEMENT) SOLE PROCEDURE,1ST LEVE	53	74	2,635	$35,558.86
E388A	Professional	VERTEBROPLSTY COMBINED WITH ANY OTHR PROCEDURE,1ST LEVEL,AD	6	15	15	$3,115.08
E391A	Professional	VERTEBROPLASTY, EACH ADDITIONAL LEVEL, ADD	25	86	159	$32,986.80

Fiscal Year 2005 - *Service Date from April 1, 2005 to March 31, 2006, Assessed from April 1, 2005 to September 30, 2006 (M7)*						
FSC	**FSC Type**	**FSC Description**	**Number of Physicians**	**Number of Patients**	**Number of Services**	**Fee Paid**
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	6	8	9	$1,613.70
TOTAL					**3,457**	**$211,259.22**
N583A	Professional	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	22	182	200	$196,827.55
N583B	Surgical Assist	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	20	67	1,351	$15,655.06
N583C	Anaesthesia	KYPHOPLSTY(BALLOON TAMP&INJECT BONE CEMENT)SOLE PROC 1ST LVL	80	125	4,009	$53,938.42
E392A	Professional	KYPHOPLASTY COMBINED WITH ANY OTHER PROCEDURE,1ST LEVEL, AD	8	15	15	$7,818.30
E393A	Professional	KYPHOPLASTY, EACH ADDITIONAL LEVEL, ADD	17	67	122	$62,903.40
E381A	Professional	INTR-OP, DIAG, OR PHYSIOLOGICAL NEURO MONITOR, ADD	6	27	28	$5,020.40
TOTAL					**5,725**	**$342,163.13**

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